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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,387	SEN ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-13,15-23,25-27 and 29-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *5,14,24 and 28* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 2-5-10.

Claims 1-41 are pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2-5-10 has been entered.

Election/Restrictions

This application contains claims 5, 14, 24, 28 are drawn to an invention nonelected with without traverse in the reply filed on 6-20-08. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections

Specification Objection and Claim Rejections - 35 USC § 112

This application does not comply with the rules for the deposit of biological material as set forth below in the Suggestion for Deposit of Biological Material. For ATCC deposits, please be sure to use the current address in Virginia, rather than the former address in Maryland.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to and claims 1-4, 6-13, 15-23, 25-27, 29-41 are rejected under *35 USC § 112*, first paragraph as failing to provide an enabling disclosure for the claimed invention.

The application discloses various biosensors that are depicted by schematics or otherwise described in Figures 1-15, that are encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material

is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The

depository is to be identified by name and address. (See 37 C.F.R. § 1.803).

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-13, 15-23, 25-27, 29-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the Office action mailed 8-5-09 and as set forth below.

Applicant's arguments filed 2-5-10 have been fully considered but they are not persuasive. Applicant argues that the specification has set forth sufficiently detailed, relevant identifying characteristics of the claimed invention such that a person skilled in the art would recognize that Applicant was in possession of the claimed subject matter. Applicant asserts that the features recited in claim 1 are described I paragraphs 10 and 52-55; Figures 1-2 and the Example commencing at paragraph 91. At paragraph 92, according to Applicant, NMR studies have confirmed that the aptamer, upon binding two molecules of adenosine, undergoes an adaptive folding forming a tightly hydrogen-bonded and stacked helical structure. Applicants' Example at paragraph 109 clearly demonstrates that the adenosine induced folded structure of the aptamer receptor was capable

of facilitating charge transfer between the first and second oligonucleotide stems. Applicant also asserts that reduction to practice has been described as to both an integrated ligand sensor as illustrated i Figure 1(b), Example 2.3.1, and a coupled ligand sensor in Figure 1(a), 15(a) and example 2.3.2, and one of skill in the art should understand that the functionality of the coupled ligand sensor does not depend on the conductivity of the aptamer domain and there is only a requirement for a conformational change in the receptor upon binding of analyte. Applicant also argues that the examiner has not addressed each of the applicant's claims separately, and that written description requirement has been satisfied in respect of each of the claims in issue, including claims directed to particular species, such as claim 29, specifically relating to an adenosine analyte. Applicant also argues that optimization of signal to noise ratios involve optimization and does not affect the operability of the invention that Applicant had possession of at the time of filing.

The specification and claims do not adequately describe the very broad genus comprising these analyte sensors. This broad genus encompasses a vast array of molecules and combination of subunits or component parts, and the disclosure fails to provide a representative number of species for the very broad genus which provide for the functions claimed, of detecting any analyte, and which sensor or sensors produce a signal upon converting to an excited, oxidized state upon a conformational change.

The specification and claims do not adequately describe the concise structural features (e.g. polynucleotide sequences, concise descriptions of the

different numbered components listed in the figures, exact structures of all component parts of the analyte sensor constructs, or those portions that are required components, those portions that are tolerated as variable components) that distinguish structures within the broadly claimed genus from those without. The specification teaches schematics of mixed or composite sensors, and some examples of analyte sensors able to detect adenosine binding by adenosine specific aptamers, and utilizing guanine doublets to monitor charge transfer to the sensor and detector stems of adenosine sensors, but the stick figures provided in the Figures do not provide enough detail for concrete, concise description of a competent biosensor structure.

Contrary to Applicant's assertions, the disclosure does not provide adequate written description for the broad genii of compounds claimed. Applicant is correct that claim 29 is drawn to a sensor which receptor site binds an adenosine analyte, but adequate written description is lacking for the genus encompassing the adenosine biosensors for the reasons set forth below. In addition, the other claims are very broadly drawn, and encompass compositions and methods of detecting the presence of any analyte comprising providing at least one analyte sensor comprising first, second, third and fourth oligonucleotide stems which are multi-stranded DNA helices, connected together at either a three way or a four way junction, and wherein at least one of the first, second, and third stems comprises a non-Watson-Crick base pairing in the vicinity of the three way junction, and/or optionally comprising a fourth oligonucleotide stem, which four stems are connected together at a four way junction, and further

comprising a receptor site which optionally binds adenosine and which site is operatively connected to the first oligonucleotide and second oligonucleotide stems and capable of binding the analyte, which sensors are alterable between conformational states, wherein a first conformational state substantially impedes charge transfer between the two oligonucleotide stems, and, upon binding of an analyte to the receptor site (which is proximate to a switch region and which switch region comprises unpaired nucleotide in a first conformational state), the sensor switches from an unexcited, unoxidized conformational state which impedes charge transfer, to one where a charge flow inducer becomes an excitable moiety in an oxidized state and forms an oxidizing agent, and which moiety is optionally rhodium III or anthraquinone, and which analyte sensor further comprises a detector which is a conductor electrically coupled to one of the oligonucleotide stems, and whereby the charge flow inducer triggers charge flow in one of the oligonucleotide stems, and a change is detected in charge transfer by electrically coupling a detector to the other one of the sensor stems, and changes are detected in the absence and presence of an analyte by measuring formation of oxidation products of the sensor, optionally including heating the sensor in the presence of piperidine and separating reaction products by gel electrophoresis.

Applicant asserts that specific designs of analyte biosensors have been successfully constructed that are alterable between a first conformational state (substantially impeding charge transfer between a first and second stem) and a second conformational state (charge is transferred between first and second

stems through a receptor site in a second conformational state) and vice versa. This rejection is based on a reading of the instant claims in light of the specification and the figures. Concise structural features are not recited in the claims, specification or figures. The figures, for instance, have structures represented by stick drawings, with little or no details about permitted or non-permitted sequences, minimum or maximum allowable lengths, or any other structural information or requisite features to allow a person of skill in the art to determine what minimal features are required for the functions claimed. There also is little or no elaboration of the concise features that are required in the different figures, and that are depicted by particular numbers (e.g. what are the concise features, characteristics, structures of numbers 10, 14, 16, 20, 22, 26 in Figure 1? What exactly do "RNA stems 14, 16, 22 and receptors 20" comprise, that are mentioned in he text on p. 15 of the specification?).

Contrary to applicant's assertions, Figures 1-15 teach generalized schematics of sensor designs, and the text of the instant disclosure advises in some instances about a lack of correlation between the proposed sensors and their ability to provide predictable strand cleavage, predictable charge transport, or predictable and sensitive analyte detection, including in the presence of various concentrations of adenosine (See, for example, pages 26-29. On page 27, for instance, first full paragraph: "…i.e. strand cleavage was observed at the proximal (P) and distal (D) guanine doublets both in the absence (lane 4) or presence (data not shown) of 2mM adenosine…"). What's more, large differences in strand cleavage and charge transfer were also observed under

different buffer conditions for the various purported sensors. See, e.g., page 28, first paragraph: "…A comparable enhancement, however, was not observed for the doublet (z) located in the third stem 22 (2-4 fold increase) as predicted by a structural model of this DNA construct…"). See also, page 29, first full paragraph: "It remains unclear whether such differences reflect purely structural transformation of the aptamer in the different ionic strength solutions or whether they also reflect changes in the process of charge-transfer through DNA."

See also the third full paragraph on p. 29: "In addition, care must be taken in interpreting the results of the adenosine dependence data from Figure 14, since the curves may not directly reflect the binding affinities of the aptamer for its ligand... and it is unclear whether the binding of only one molecule of ligand allows charge transfer to occur to some extent or not."

While some details are provided for the concept of sensors in the instant disclosure, concise structural features of a representative number of species of the claimed genii are lacking. The specification and claims do not adequately describe the very broad genus comprising these analyte sensors. This broad genii encompass a vast array of molecules and combination of subunits or component parts, and the disclosure fails to provide a representative number of species for the very broad genii which provide for the functions claimed, of predictably and accurately detecting any analyte, and which sensor or sensors reliably produce a signal upon converting to an excited, oxidized state upon a conformational change. The specification and claims do not adequately describe the concise structural features (e.g. polynucleotide sequences, structures of all

component parts of the analyte sensor constructs) that distinguish structures within the broadly claimed genus from those without. The specification teaches schematics of mixed or composite sensors, and some examples of analyte sensors able to detect adenosine binding by adenosine specific aptamers, and utilizing guanine doublets to monitor charge transfer to the sensor and detector stems of adenosine sensors.

See also page 32, first full paragraph of the instant specification: "The ATP aptamer described in this Example possesses a dissociation constant in the mM range for the adenosine ligand. Such a binding affinity would be insufficient for a practical sensor intended to monitor, for instance, hormone levels in blood (for which, sensor-analyte affinities in the low nM to high pM range would be required." And, while the disclosure predicts that aptamers can be obtained using methods previously identified in the art, such as the SELEX method, a concise description of the actual construction of sensor molecules comprising analyte binding sites, and allowing predictable conformational changes in the presence of analytes in a solution that render predictable charge transfer and measurable signals, has not been provided. Written description takes into consideration what Applicant had in his possession at the time of filing, not what future experiments might produce. It is unclear from what has been provided in the text, the figures and the claims, what minimal structural requirements are set forth for a functional biosensor to switch between permissive and non-permissive charge transfer upon binding to an analyte.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species, requisite sequences, structural components, higher order structures, or any concrete descriptions of the necessary physical parameters of the sensors depicted in the figures to describe the very broad genii comprising at least one analyte sensor comprising first, second, third and fourth oligonucleotide stems which are multi-stranded DNA helices, a receptor site which optionally binds any analyte and which site is operatively connected to the first oligonucleotide and second oligonucleotide stems and capable of binding any analyte, which sensors are predictably alterable between conformational states, wherein a first conformational state substantially impedes charge transfer between the two oligonucleotide stems, and, upon binding of any analyte to the receptor site, switches from an unexcited, unoxidized conformational state which impedes charge transfer, to one where a charge flow inducer becomes an excitable moiety in an oxidized state, and which provides for the function of detecting any analyte. The description provided in the instant disclosure does not adequately describe the elements, structures or sequences required for the broad genii claimed.

Thus, one of skill in the art would reasonably conclude that Applicant was not in possession of the broadly claimed genus. For these reasons, the instant rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6-13, 15-23, 25-27, 29-41 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 of copending Application No. 12/102,669 for the reasons of record set forth in the Office action mailed 10-16-08. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to compositions and methods of detecting the presence of any analyte comprising providing at least one analyte sensor comprising first and second oligonucleotide stems, and further comprising a receptor site which binds an analyte, and which site is operatively connected to the first oligonucleotide and second oligonucleotide stems and capable of binding the analyte, which sensors are alterable between conformational states, wherein

a first conformational state substantially impedes charge transfer between the two oligonucleotide stems, and, upon binding of an analyte to the receptor site (which is proximate to a switch region and which switch region comprises unpaired nucleotide in a first conformational state), the sensor switches from an unexcited, unoxidized conformational state which impedes charge transfer, to one where a charge flow inducer becomes an excitable moiety in an oxidized state and forms an oxidizing agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No arguments were made addressing this rejection.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the

examiner's supervisor, Fereydoun Sajjadi, can be reached on (571) 272-3311. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
4-9-10

/Jane Zara/

Primary Examiner, Art Unit 1635